

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on 3-25-04

QUINE INTELLECTUAL PROPERTY LAW GROUP, P.C.

By: Thacie Brooks

**AFFIDAVIT OF INVENTOR JOHN A. ANGELOS
UNDER 37 C.F.R. § 1.131**

Appl. No. : 09/884,696 Confirmation No.: 4037
Applicant : Lisle W. George, *et al.*
Filed : June 19, 2001
TC/A.U. : 1645
Examiner : Virginia Allen Portner

Docket No. : 407J-000700US
Customer No. : 22798
Client Ref No.: 1999-069-1

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, John A. Angelos, am a named inventor on U.S. Patent Application Serial No. 09/884,696, filed in the USPTO on June 19, 2001, cited above. I am currently employed in the Department of Veterinary Medicine and Epidemiology in the School of Veterinary Medicine at the University of California, Davis.

The invention described in the specification of the case cited above pertains, in part, to the cytotoxin protein (referred to as MbxA) and gene (referred to as mbxA) from the pathogenic bacteria *Moraxella bovis*. The *M. bovis* organism is the causative agent of infectious bovine keratoconjunctivitis (IBK), and is responsible for significant economic losses in the cattle industry. The invention provides compositions and methods finding a variety of uses, including but not limited to the diagnosis, prevention and treatment of IBK, as well as finding use in the scientific study of this disease and its causative agent, *M. bovis*.

I have read the Office Action dated November 15, 2002, and understand that the Examiner has rejected all pending claims under 35 U.S.C. § 102(a) for alleged anticipation by PCT publication WO 01/16172 to Farn *et al.*, published on March 8, 2001. The Examiner alleges that the cytotoxin provided by Farn *et al.* anticipates the MbxA cytotoxin and cytotoxin fragments provided by the present invention.

I point out that the cytotoxin gene and polypeptide provided in PCT publication WO 01/16172 is not the gene and polypeptide taught by Application Serial No. 09/884,696. The gene taught in Application Serial No. 09/884,696 has a guanosine at nucleotide position 1096 (see FIG. 3 and SEQ ID NO: 1), whereas the PCT publication teaches a cytotoxin gene with an adenosine at that same position (see FIG. 5 and SEQ ID NO: 6 in that publication). As a result of this difference in nucleotide sequence, the respective proteins have different amino acid sequences; the Applicants invention provides a cytotoxin protein with an alanine at amino acid position 366 (see SEQ ID NO: 2 in that specification), whereas the cited PCT publication teaches a cytotoxin with a threonine at this position (see SEQ ID NO: 5 in that publication).

Furthermore, I and the other two named inventors fully conceived and reduced to practice the claimed invention (*i.e.*, the mbxA cytotoxin gene and protein sequences) in the United States of America prior to the publication of WO 01/16172 on March 8, 2001. The attached Exhibits provide evidence of the conception of the invention and its reduction to practice prior to March 8, 2001.

Exhibit A provides a copy of a scientific paper entitled "Cloning and characterization of a *Moraxella bovis* cytotoxin gene," published in the American Journal of Veterinary Research, Vol. 62, No. 8, p. 1222-1228; August 2001. The paper is authored by John F. Hess, Lisle W. George and myself, who are also the three inventors listed on the present application. The AJVR manuscript was submitted to AJVR for review on August 25, 2000, as shown on page 1222 at the bottom of the left column. The manuscript cites GenBank Accession No. AF205359 (page 1225, right column, third paragraph), which provides sequences of the MbxA gene and protein.

Exhibit B provides a copy of the submission in GenBank with Accession No. AF205359. On page one of this GenBank listing it is shown that the MbxA protein sequence identical to the sequence provided in Application Serial No. 09/884,696, SEQ ID NO: 2, was first submitted to GenBank on November 15, 1999. Although the sequence was submitted to GenBank on

November 15, 1999, it was withheld for release until August 2001 to coincide with publication of the AJVR article.

Exhibit C provides a color copy of the GenBank Accession No. AF205359 Sequence Revision History. On page one of this history, it is shown that there have been two revisions following the original submission on November 15, 1999. These revisions are dated October 2, 2001 and June 23, 2003, and are color-coded in purple and pink, respectively. Page three of the Sequence Revision History indicates that no revision of the MbxA protein sequence has been made since its original submission on November 15, 1999.

Exhibit D provides a copy of an email correspondence from the National Center for Biotechnology Information (NCBI) to myself. This correspondence confirms my request for a delayed release of the sequence information submitted to GenBank on November 15, 1999. As seen in the email, the sequence was held until the earlier of either November 30, 2001 or the publication of the aforementioned AJVR manuscript. The AJVR manuscript was published in August 2001, and GenBank Accession No. AF205359 was made public at that time.

Exhibits A, B, C and D demonstrate that the claimed invention (including the MbxA protein sequence) was conceived and reduced to practice by the listed inventors on Application Serial No. 09/884,696 before the publication of WO 01/16172 on March 8, 2001.

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.


John A. Angelos

Dated: 3-21-04